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## BIOLOGICAL SAFETY IN THE ANIMAL LABORATORY<sup>1</sup>

G. BRIGGS PHILLIPS AND JOSEPH V. JEMSKI<sup>2</sup>

**ABSTRACT.** Biological hazards for animal room personnel can be controlled through vaccination, the use of correct techniques, the use of safety apparatus, the design of laboratories, and by certain management functions related to selecting, training, and supervising personnel. Selection of the approaches to the laboratory safety program is a matter to be decided by each laboratory director. Proper application of these approaches should contribute to over-all control of laboratory environment and to the ability of the animal laboratory to perform its function efficiently and without interruption.

Hazards in the animal laboratory fall into three principal categories: 1) those that cause physical injuries, cuts, burns, explosions, and fires; 2) those that cause radiation exposure; and 3) those that cause laboratory-acquired illnesses. This paper deals with the third category. Its purpose is to present a brief synopsis of the present day situation and to suggest approaches for the control of biological hazards. Some of the information is based on the results of a study of biological laboratory safety in 102 laboratories in the United States and in 17 foreign countries.

Biological laboratory safety is not a subject restricted to the interests of those who use animals in infectious disease experimentation. Any use of laboratory animals introduces a possible biological hazard element if for no other reason than that animals may carry a latent infection which they may transfer to man. Conversely, it is also possible that organisms contributed by man may cause disease in the animal colony. If not handled properly, animals may inflict trauma on their handlers through bites and scratches, and these wounds may become infected. Also, when one considers the different types of personnel who handle animals and the multitude of laboratory operations that involve animals, their tissues, or their excreta, it becomes clear that animal laboratory safety is difficult to separate from the larger field of laboratory safety.

### SURVEYS OF LABORATORY INFECTIONS

A starting point for the discussion is to ask if occupationally-acquired infections are a problem in the infectious disease laboratory. The answer seems to be "yes." The Germans were publishing collected cases of infections acquired in the laboratory as early as 1915. In a survey completed by one of us (G. B. P.) in 1960, there was a total of 426 laboratory infections occurring in 102 laboratories in 18 countries over a period of approximately ten years. Animals were used in 90% of these laboratories. Data from this survey are shown in Table 1.

The frequency of laboratory illnesses among the three types of laboratories

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<sup>2</sup> U.S. Army Chemical Corps Biological Laboratories, Fort Detrick, Frederick, Maryland.

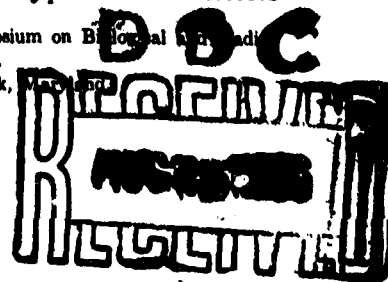


TABLE 1

*Laboratory infections in 102 laboratories*

Laboratories listing infections	65
Total infections listed	426
Number of fatalities	17
Number of infectious agents involved	31
Laboratories which had infections but which did not list them	12
Laboratories having no infections	25

TABLE 2

*Infection rates in 102 laboratories according to type of laboratory*

Type of Laboratory	Per cent having infections	Infections per laboratory
Commercial or private	62	3.53
Educational institute	53	4.29
Government or state operated	75	9.63

TABLE 3

*Sources of 1087 cases of laboratory infections\**

	Number	Per cent
Known accidents	213	19.6
Worked with the agent	271	24.9
Clinical specimens	175	16.1
Aerogenic	173	16.0
Cleaning	20	1.8
Infected animals or ectoparasites	137	12.6
Performing autopsies	98	9.0

\* After Pike and Sulkin, 1952.

represented in the survey is shown in Table 2. The most frequently occurring laboratory-acquired diseases were tuberculosis, Q fever, brucellosis, psittacosis, and tularemia. It is significant that 73 of the 102 laboratories kept no written records of infections and 92 kept no records of accidents. Thus the 426 infections are probably only a part of those that actually occurred. The higher frequency of illnesses in government or state operated laboratories was due to larger exposed populations handling larger volumes of infectious materials.

A number of other publications have dealt with collections of cases of laboratory infections. To date the largest available body of information is the survey published by Pike and Sulkin (1952), which dealt with infections occurring in U.S. laboratories during a 20-year period. We can generally indicate from this study how frequently animals were involved in the human infections, but it is not possible to make an accurate comparison between hazards in laboratory work involving and not involving animals. Table 3 shows how the cases were

TABLE 4  
*Known and unknown causes of infection in an infectious disease institute\**

	Percentage	
	Known cause	Unknown cause
From Sulkin and Pike survey	16-20	84-80
From survey in 18 countries	14	86
Detrick safety division reports 1950-6	30	70
Detrick supervisor's written reports 1953-6	33	67
Exhaustive investigation of cases 1955-57	35	65
Detrick mechanical and chemical lost-time injuries	100	0

\*Adapted from Wedum, 1959.

categorized based on the nature of the work in which the infected persons were involved. Animals were directly involved in two categories and together these accounted for about 22% of the total. In addition, 32 of the 213 "known accidents" were accidents also involving animals. Unfortunately we cannot tell to what extent animals may have been secondarily involved in the other categories. It is probably safe to say, however, that animals were involved in some way in from 30-40% of the infections.

Note that only 213 of the 1087 cases were attributed to *known* accidents. This is most important because it means if one attempts to determine what were the unsafe acts or the unsafe conditions, over three-fourths of the cases are put in an "unknown" category. This result is typical of most surveys of laboratory infections. It is further illustrated in Table 4 (Wedum, 1959) where the results of the Sulkin and Pike survey and the foreign survey are listed as well as the results obtained when special efforts were made at Fort Detrick to search out these unknown causes. Notice, by contrast, that the unsafe act or the unsafe condition could always be found with the mechanical and chemical lost-time injuries.

#### LABORATORY HAZARDS STUDIES

A reasonable conclusion that can be reached from the above data is that some procedures carried out in the laboratory create unsuspected hazards for operating personnel. Indeed this observation has been confirmed by a number of studies in which measurement has been made of the amount of microbial aerosol produced by various laboratory techniques. Most of the common techniques have been tested in this manner in studies done in this country (Reitman and Wedum, 1956; Barbeito, Alg, and Wedum, 1959) and in England (Tomlinson, 1957; Whitwell, Taylor, and Oliver, 1957). They show that most common laboratory techniques carried out in the ordinary manner will from time to time produce infectious air-borne particulates. At least one study has shown that these air-borne particulates are of a size which will readily penetrate to the human lung if they are breathed (Tomlinson, 1957). Of course, it is recognized that these results only

suggest possible means of laboratory infection. The type of microorganism, its probable infectious dose, its environmental resistance, the resistance of the host, and many other factors would have to be evaluated for accurate quantitation of a hazard.

Animal cross-infection experiments have provided another means of detecting possible human infectious hazards in the animal room. A number of studies have been recently summarized by Kirchheimer, Jemski, and Phillips (1961), which show that cross-infection often can and does occur. Again, demonstrating the infection of control animals housed in infectious animal rooms is not a direct measure of human hazards, but it is an indication that infectious agents are present in the environment.

#### APPROACHES TO THE PROBLEM

A general conclusion from the above studies is that biological safety is largely a matter of environmental control. Since it is difficult to determine what might be an allowable contamination level of an infectious agent in the same way that allowable limits are set for radiation exposure and for exposure to certain air pollutants, the usual practice is to strive for complete environmental control. This is especially true for diseases with severe consequences or for those for which there is no treatment.

Insofar as accident prevention is an environmental control problem, it becomes apparent that solutions require that we deal simultaneously with a series of interlocking factors (Stead, 1961). This means that what we want to do is to use a "systems approach" to safety which consists of man, his environment, and accident agents. This is sometimes referred to as the epidemiological approach because the ecology of the situation is examined and manipulated so as to put man in a favorable survival position. A number of interacting forces can be considered in any one situation.

For example, in the field of traffic safety it has been suggested that the system consists of the driver, the vehicle, the highway, and the pedestrian. Likewise, in vector-borne disease control the system is composed of the etiological agent, the vector, the reservoir, and the susceptible human host. Following this line of thinking one could say that in the animal laboratory the system is composed of the following elements: man, animals, infectious agents, the procedures and techniques used, the equipment used, and the building facilities present.

But how does one achieve the environmental control needed for biological safety in the animal laboratory? What approaches can be used in controlling laboratory hazards? We have listed five approaches.

##### 1. Vaccination

Vaccination of laboratory personnel is recommended when a satisfactory immunogenic preparation is available. Good immunity is conferred after vaccination against smallpox, tetanus, yellow fever, botulism, and diphtheria.

Other vaccines such as those for psittacosis, Q fever, tularemia, Rift Valley fever, and anthrax have been or are being tried experimentally with varying degrees of success. But vaccines have not been as yet developed for a number of human diseases which have been known to occur in laboratory workers. Among these are dysentery, blastomycosis, brucellosis, coccidioidomycosis, glanders, histoplasmosis, infectious hepatitis, leptospiroses, and toxoplasmosis. Moreover, we generally evaluate the efficiency of vaccines for laboratory workers on the basis of their effectiveness in preventing disease in the general population. Two possible pitfalls to this line of thinking should be mentioned. The first is that the laboratory worker may be exposed to infectious microorganisms at a higher dose level than would be expected from normal public exposure. Secondly, this exposure may be by a route different from that normally expected, e.g., respiratory infection with the tularemia or anthrax organism.

### *2. Techniques and Procedures*

Many procedural rules for laboratory safety are obvious. Avoid mouth pipetting of infectious or toxic fluids. Use only needle-locking syringes. Sterilize all contaminated discard material. Frequently disinfect hands and working surfaces. Do not smoke, eat, or drink in the laboratory. These rules certainly are well known and should be observed.

Other procedural rules may be less well understood and require more explanation. Do not blow out the last drop from the pipette. Do not mix dilutions by blowing air through the pipette into the culture. Wear gloves when handling infectious fluids in a syringe. Use an alcohol-soaked pledget when removing a syringe and needle from a rubber-stoppered vaccine bottle. There are a number of others having to do with procedures such as centrifuging, grinding tissue, lyophilizing, caging animals, etc., which are, for the most part, pointed toward eliminating air-borne contamination of the laboratory environment. Once the fundamental concepts of how easily aerosols may be produced by ordinary laboratory techniques are understood, the laboratory supervisor should attempt to design safety into new procedures and new tests which are developed, the idea being to eliminate or to modify those steps or manipulations which are the most hazardous.

### *3. Safety Equipment*

The most important single piece of safety equipment in the infectious disease laboratory is the ventilated work cabinet. The basic requirements for such a cabinet are 1) sufficient inward air flow (at least 50 linear ft per min) or operation at a negative pressure, 2) filtration of exhaust air, and 3) means of sterilizing both the exhaust filter and the interior of the cabinet.

Other types of safety equipment have been developed for safely carrying out certain procedures such as blending and centrifugation. Some have been designed to facilitate certain operations in ventilated work cabinets. Much equip-

ment is commercially available and source information can be made available. A partial list of safety equipment would include inoculating loop incinerators, pipettor devices, safety centrifuge cups, safety blender bowls, and filter masks. The latter are mentioned because of the well-known inefficiency of the common hospital gauze mask in filtering out air-borne particles. Filter masks with high filtering efficiencies suitable for laboratory or animal room work are now available. However, since the ventilated cabinet externalizes an entire working area instead of the worker, it is generally the first type of safety equipment which should be provided.

Some people might claim we have relied too heavily on mechanical equipment. What is known is that equipment alone will not solve all the safety problems. Wedum (1959) has shown how at a biological research institution the use of safety equipment such as ventilated animal cages and ventilated cabinets resulted in a reduction of the biological accident and illness rates only to a certain point where a plateau or steady state was reached. Further reduction of the infectious risks, it was felt, depended upon a "human factors" approach to accident prevention.

#### *4. Building Facilities*

Construction criteria for laboratories which augment and improve safety have been developed and are available (Wedum *et al.*, 1956). More and more, as demands upon the laboratory scientists increase, certain building design features cease to be mere advantages in animal work and become necessities. Among these may be mentioned 1) building ventilation, 2) control of direction of air movement, 3) biological filtration of air, 4) physical separation of areas of different risk level, and 5) use of germicidal gases and radiations. Modern construction criteria for laboratories and animal rooms do much to reduce infectious risks and to prevent laboratory infections.

#### *5. Management Aspects*

Included in this category would be such essential elements as programming for safety, selection of proper personnel, safety training of personnel, use of safety regulations, and reporting and investigation of accidents. The management approach also attempts to include control of human factors in accident causation and attempts to provide an atmosphere wherein personnel may develop attitudes conducive to safe performance. There are no easy answers as to how the management aspects of biological safety should be applied. Practical experience, however, has shown that they must be given some attention for an accident and infection prevention program to be successful. Of course, it must be obvious that good management of an animal laboratory includes good safety management. Safety is only one of management's aims, but it is an essential part of any productive enterprise.

Any program of loss-prevention is based on the dual premise that 1) the loss

(in this case laboratory-acquired illness) is the result of a series of events which result in an accident and 2) accidents are largely preventable by controlling these events. Translated into terms of our own problem it simply means this:

a) Accidents or wrong techniques create conditions for infection. Remember that the techniques may not be recognized as being wrong because, from the biological point of view, they may not have been "safety tested."

b) If the accident were preceded by any predisposing human or physical factors, these must be corrected in order to prevent the accident which causes the infection.

The following are a few suggestions for the management approach to the control of laboratory hazards. These are pointed toward the real focal point of the laboratory—the laboratory workers.

- 1) Establish written safety regulations that are read and understood by all.
- 2) Keep the safety needs in mind when screening and selecting new employees.
- 3) Train each new employee until it is certain that he understands the rules and why.
- 4) Inasmuch as possible, design safety into techniques and procedures as they are developed.
- 5) Establish responsibility for safety. Each supervisor should be responsible for the safety of his people, but each employee should have a personal responsibility—safety should be a part of every job.
- 6) Establish a reporting system for accidents, lost-time injuries, and infections and insist on prompt reporting.
- 7) Investigate each illness and each accident to determine what should be done to prevent recurrence.
- 8) Encourage workers at all levels to suggest means of eliminating laboratory hazards.

#### CONCLUSION

It is understandable that not all laboratories would need to employ all of the suggestions made in this paper. These suggestions are merely a composite of the approaches used to control laboratory hazards in a large number of laboratories. Some approaches can be applied in any laboratory because no expenditure of funds is required. Selecting how much of each approach should make up the laboratory safety program is obviously a matter to be decided by each laboratory director. It is desirable, however, for infection prevention to be a natural consequence of the efforts of all concerned to have an efficient and productive laboratory.

Modern-day research and medical practices should be supported by animal laboratory services which are just as modern. Control of laboratory-infectious risks through vaccination, the use of correct techniques, the use of safety apparatus, the design of laboratories, and by certain management functions, contributes to over-all control of laboratory environment and thus to the ability

of the laboratory to perform its proper function efficiently and without interruption.

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